A Nucleotide Analogue Induced Gain of Function Corrects the Error-Prone Nature of Human DNA Polymerase Iota

Amit Ketkar, Maroof K. Zafar, Surajit Banerjee[§], Victor E. Marquez[#], Martin Egli[¶] and Robert L. Eoff*

From the Department of Biochemistry and Molecular Biology

University of Arkansas for Medical Sciences, Little Rock, Arkansas 72205-7199, USA

§*Northeastern Collaborative Access Team & Department of Chemistry & Chemical Biology, Cornell University, Argonne National Laboratory, Argonne, Illinois 60439, USA*

#*Chemical Biology Laboratory, Center for Cancer Research*

National Cancer Institute at Frederick

Frederick, Maryland 21702, USA

¶*Department of Biochemistry, Vanderbilt University School of Medicine, Nashville, Tennessee, 37232-0146*

Address correspondence to:

Robert L. Eoff

Department of Biochemistry & Molecular Biology

University of Arkansas for Medical Sciences

325 Jack Stephens Drive

Little Rock, Arkansas 72205-7199

Telephone: (501) 686-8343

Fax: (501) 686-8169

E-mail: RLEOFF@UAMS.EDU

Running Title: Structural basis for modulation of Y-family DNA polymerase activity by fixed conformation 2'-deoxy-bicyclo[3.1.0]hexane nucleosides

SUPPORTING INFORMATION

Table 1: Crystal data and refinement parameters

Parameter	**iota North**	**iota South**	**iota dATP**
X-ray source	APS	APS	APS
Beamline	ID24-E	ID24-E	ID24-E
Detector	ADSC Q315	ADSC Q315	ADSC Q315
Wavelength (Å)	0.979	0.979	0.979
Temperature (K)	110	110	110
No. of Crystals	1	1	1
Space group	$P6_522$	$P6_522$	$P6_522$
Unit Cell (a, b, c; Å)	97.8,97.8,203.6	97.8,97.8,202.7	98.2,98.2,202.1
Resolution range (Å)	48.8-2.90	48.8-2.57	44.2-2.10
Highest resolution shell[a]	(3.01-2.90)	(2.66-2.57)	(2.20-2.10)
No. of measurements	205169	322554	292725
No. of unique reflections	14931 (1448)	19039 (1829)	34481 (3340)
Redundancy	7.0 (7.2)	6.4 (5.7)	5.3 (5.2)
Completeness (%)	95.1 (86.0)	99.9 (92.3)	93.3 (86.0)
R-merge[b] (%)	4.5 (65.7)	6.7 (40.9)	8.7 (61.7)
Signal to noise (I/sI)	24.6 (1.9)	51.5 (5.3)	24.5 (1.6)
Model Composition			
No. of amino acid residues	376	376	376
No. of water molecules	78	104	334
No. of Ca^{2+} ions	3	3	3
No. of template nucleotides	9	9	9
No. of primer nucleotides	7	7	7
No. of dATP/MC-dATP	1	1	1
R_f[c] (%)	20.4	20.4	22.0
R-$_{free}$[d] (%)	25.1	26.2	26.5
Temperature factors			
From Wilson plot (Å^2)	59.1	52.2	36.3
r.m.s. standard deviation from ideal values			
Bond lengths (Å)	0.015	0.008	0.011
Bond angles (°)	1.4	1.2	1.4
Dihedral angles (°)	18.9	17.2	17.0

[a] Values in parentheses correspond to the highest resolution shells.

[b] R-merge = $\Sigma_{hkl}\Sigma_{j=1,N}|\langle I_{hkl}\rangle - I_{hkl,j}| / \Sigma_{hkl}\Sigma_{j=1,N}|I_{hkl,j}|$, where the outer sum ($hkl$) is taken over unique the reflections.

[c] $R_f = \Sigma_{hkl}||F_{o,hkl}| - k|F_{c,hkl}||/\Sigma_{hkl}|F_{o,hkl}|$, where $|F_{o,hkl}|$ and $|F_{c,hkl}|$ are the observed and calculated structure factors, respectively.

[d] R_{free} *idem*, for the set of reflections (10% of the total) omitted from the refinement process.